PATENT COOPERATION TREATY

From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To:
THOMAS A. CAWLEY, JR.
PILLSBURY WINTHROP LLP
P.O. BOX 10500
MCLEAN, VA 22102

PCT

NOTIFICATION OF TRANSMITTAL OF INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Rule 71.1)

Date of Mailing *(day/month/year)*	06 DEC 2004
Applicant's or agent's file reference 37003-304483	**IMPORTANT NOTIFICATION**

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/US03/19652	23 June 2003 (23.06.2003)	21 June 2002 (21.06.2002)

Applicant

IDEC PHARMACEUTICALS CORP.

1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary examination report and its annexes, if any, established on the international application.

2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.

3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.

4. **REMINDER**

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices)(Article 39(1))(see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.

Name and mailing address of the IPEA/US Mail Stop PCT, Attn: IPEA/US Commissioner for Patents P.O. Box 1450 Alexandria, Virginia 22313-1450 Facsimile No. (703)305-3230	Authorized officer David J Blanchard DEBORAH A. THOMAS PARALEGAL SPECIALIST GROUP 1800 Telephone No. (571) 272-0827

Form PCT/IPEA/416 (July 1992)

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 37003-304483	**FOR FURTHER ACTION**	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/US03/19652	International filing date *(day/month/year)* 23 June 2003 (23.06.2003)	Priority date *(day/month/year)* 21 June 2002 (21.06.2002)
International Patent Classification (IPC) or national classification and IPC IPC(7): C07K 16/00; A61K 39/395 and US Cl.: 530/387.1, 387.3, 388.1; 424/130.1, 133.1, 181.1, 183.1		
Applicant IDEC PHARMACEUTICALS CORP.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 6 sheets, including this cover sheet.

   ☐ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of ___ sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the report
   - II ☐ Priority
   - III ☐ Non-establishment of report with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - VI ☒ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☐ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
14 January 2004 (14.01.2004)	01 December 2004 (01.12.2004)
Name and mailing address of the IPEA/US Mail Stop PCT, Attn: IPEA/US Commissioner for Patents P.O. Box 1450 Alexandria, Virginia 22313-1450 Facsimile No. (703)305-3230	Authorized officer David J Blanchard Telephone No. (571) 272-0827 DEBORAH A. THOMAS PARALEGAL SPECIALIST ~~GROUP 1800~~

Form PCT/IPEA/409 (cover sheet)(July 1998)

INTERNATIONAL PRELIMI[redacted] EXAMINATION REPORT

International a[redacted]cation No.
PCT/US03/19[redacted]

I. Basis of the report

1. With regard to the **elements** of the international application:*

☒ the international application as originally filed.

☒ the description:
pages 1-24 as originally filed
pages NONE , filed with the demand
pages NONE , filed with the letter of _____.

☒ the claims:
pages 25-38 , as originally filed
pages NONE , as amended (together with any statement) under Article 19
pages NONE , filed with the demand
pages NONE , filed with the letter of _____.

☒ the drawings:
pages 1-7 , as originally filed
pages NONE , filed with the demand
pages NONE , filed with the letter of _____.

☐ the sequence listing part of the description:
pages NONE , as originally filed
pages NONE , filed with the demand
pages NONE , filed with the letter of _____.

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.
These elements were available or furnished to this Authority in the following language _____ which is:

☐ the language of a translation furnished for the purposes of international search (under Rule23.1(b)).

☐ the language of publication of the international application (under Rule 48.3(b)).

☐ the language of the translation furnished for the purposes of international preliminary examination(under Rules 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

☐ contained in the international application in printed form.

☐ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority in written form.

☐ furnished subsequently to this Authority in computer readable form.

☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. ☐ The amendments have resulted in the cancellation of:

☐ the description, pages NONE

☐ the claims, Nos. NONE

☐ the drawings, sheets/~~fig~~ NONE

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).**

** Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17).*

*** Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.*

INTERNATIONAL PRELIMI[redacted]Y EXAMINATION REPORT

International [redacted]cation No.
PCT/US03/1[redacted]

V. Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. STATEMENT

Novelty (N)	Claims Please See Continuation Sheet	YES
	Claims Please See Continuation Sheet	NO
Inventive Step (IS)	Claims Please See Continuation Sheet	YES
	Claims Please See Continuation Sheet	NO
Industrial Applicability (IA)	Claims Please See Continuation Sheet	YES
	Claims Please See Continuation Sheet	NO

2. CITATIONS AND EXPLANATIONS
Please See Continuation Sheet

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International [redacted]cation No.
PCT/US03/19652

VI. Certain documents cited

1. Certain published documents (Rule 70.10)

Application No Patent No.	Publication Date *(day/month/year)*	Filing Date *(day/month/year)*	Priority date (valid claim) *(day/month/year)*
US 2003/0113316 A1	19 June 2003 (19.06.2003)	25 July 2002 (25.07.2002)	25 July 2001 (25.07.2001)
US 2003/0138417 A1	24 July 2003 (24.07.2003)	08 November 2002 (08.11.2002)	08 November 2001 (08.11.2001)

2. Non-written disclosures (Rule 70.9)

Kind of non-written disclosure	Date of non-written disclosure *(day/month/year)*	Date of written disclosure referring to non-written disclosure *(day/month/year)*

Supplemental Box
(To be used when the space in any of the preceding boxes is not sufficient)

V.1. Reasoned Statements:
The opinion as to Novelty was positive (Yes)with respect to claims 13, 15-17, 19, 33, 35-39, 53, 55-59, 73, 75-79, 94-98, 102-121
The opinion as to Novelty was negative (No) with respect to claims 1-12, 14, 18-19, 32, 34, 40-52, 54, 60-72, 74, 80-93, 99-101
The opinion as to Inventive Step was positive (Yes)with respect to claims NONE
The opinion as to Inventive Step was negative(NO) with respect to claims 1-121
The opinion as to Industrial Applicability was positive (YES) with respect to claims 1-121
The opinion as to Industrial Applicability was negative(NO) with respect to claims NONE

Claims 1-12, 14 and 18-19 lack novelty under PCT Article 33(2) as being anticipated by Kakuta et al.

Claims 1-12, 14 and 18-19 are drawn to antibody compositions consisting essentially of histidine or acetate buffer at concentration ranges of 2mM to about 48mM; 3mM to about 48mM, 4mM to about 45mM; 5mM to about 40mM; 20mM to about 25mM and the pH is in the range from about 4-7.5; 4.5-7; 5-6.5; 5.5-6 and the antibodies are chimeric or humanized and the concentration of the antibodies is at least 50 mg/mL and at least 100 mg/mL.

Kakuta et al teach antibody compositons in histidine buffer having various concentration ranges that overlap or touch the claimed buffer concentration ranges (e.g., see pages 4-6 and example 6) as well as the claimed pH ranges and the antibodies are chimeric or humanized (see pages 7-8) and the antibodies are preferably at least 100 mg/mL (see page 13). The teachings of Kakuta et al are sufficiently specific that the skilled artisan would readily envisage the instantly claimed buffer concentrations, pH values, and antibody concentrations from the teachings of Kakuta et al.

Claims 1-12, 14, 18, 20-32, 34, 40-52, 54, 60-72, 74, 80-93 and 99-101 lack novelty under PCT Article 33(2) as being anticipated by Lam et al

The claims have been described supra. Claims 20-32, 34, 40-52, 54, 60-72, 74, 80-93 and 99-101 are drawn to the antibody compositions that comprise antibodies that binds specific antigens (i.e., CD4, CD20) and a method for producing a concentrated antibody compositions by subjecting the initial antibody preparation to membrane filtration, wherein the antibody compositions are in histidine or acetate buffers having the previously said concentration ranges and pH ranges. The concentrated antibody compositions may further comprise one or more pharmaceutically acceptable carriers to produce a pharmaceutical composition. The claims also encompass an improved method of therapy that includes administration of said pharmaceutical composition comprising said antibody compositions for treating a patient having cancer, allergic disorders, autoimmune diseases or lymphoma.

Lam et al teach antibody compositions and pharmaceutical compositions comprising monoclonal antibodies, chimeric or humanized antibodies in histidine or acetate buffers having a pH in the pH range from about 4.5-about 6.0, most preferably of about pH 5.0 and the pharmaceutical compositions comprise one or more pharmaceutically acceptable carriers, excipients or stabilizers (see entire document especially bridging paragraph of columns 22-23, columns 5-9 and 22-23 and Tables 1, 15 and 16). Lam et al teach an antibody composition comprising an anti-CD20 antibody in 25mM histidine at pH5, 6.5 or 7.5 (see Figure 24 and legend at column 4). Applicant is reminded that when by a recitation of ranges or otherwise, a claim covers several compositions, the claim is anticipated if one of them is in the prior art. See MPEP 2131.03. Lam et al teach antibody concentration using a protein concentration filter/ultrafiltration unit (see column 21, lines 33-37). Lam et al teach a method of therapy comprising administering said pharmaceutical compositions to a patient (preferably human; column 23, line 33) for treating disorders including rheumatoid arthritis (see column 24) (see columns 23-24).

Supplemental Box
(To be used when the space in any of the preceding boxes is not sufficient)

Claims 1-121 meet the criteria set out in PCT Article 33(4), and thus have industrial applicability because the subject matter claimed can be made or used in industry.

----------NEW CITATIONS----------

US 6,171,586 B1 (LAM et al) 9 January 2001, see entire document, especially bridging paragraph of columns 6-7, columns 7-10, 21-24, Table 1 and examples.

PATENT COOPERATION TREATY

From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To:
THOMAS A. CAWLEY, JR.
PILLSBURY WINTHROP LLP
P.O. BOX 10500
MCLEAN, VIRGINIA 22102

PCT

NOTIFICATION OF RECEIPT
OF DEMAND BY COMPETENT INTERNATIONAL
PRELIMINARY EXAMINING AUTHORITY

(PCT Rules 59.3(e) and 61.1(b), first sentence
and Administrative Instructions, Section 601(a))

Date of mailing *(day/month/year)*: 24 MAY 2004

Applicant's or agent's file reference: 37003-304483

IMPORTANT NOTIFICATION

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/US03/19652	23 Jun 2003	21 Jun 2002

Applicant: IDEC PHARMACEUTICALS CORP.

1. The applicant is hereby **notified** that this International Preliminary Examining Authority considers the following date as the date of receipt of the demand for international preliminary examination of the international application:

   14 JAN 04

2. That date of receipt is:

   [X] the actual date of receipt of the demand by this Authority (Rule 61.1(b)).

   [ ] the actual date of receipt of the demand on behalf of this Authority (Rule 59.3(e)).

   [ ] the date on which this Authority has, in response to the invitation to correct defects in the demand (Form PCT/IPEA/404), received the required corrections.

3. [ ] **ATTENTION:** That date of receipt is **AFTER** the expiration of 19 months from the priority date. Consequently, the election(s) made in the demand does (do) not have the effect of postponing the entry into the national phase until 30 months from the priority date (or later in some Offices) (Article 39(1)). Therefore, the acts for entry into the national phase must be performed within 20 months from the priority date (or later in some Offices) (Article 22). For details, see the *PCT Applicant's Guide*, Volume II.

   [ ] *(If applicable)* This notification confirms the information given by telephone, facsimile transmission or in person on:

   _____

4. Only where paragraph 3 applies, a copy of this notification has been sent to the International Bureau.

Name and mailing address of the IPEA/	Authorized officer
Mail Stop PCT, Commissioner for Patents P.O. Box 1450, Alexandria, VA 22313-1450	Melvin Brooks, Sr.
Facsimile No. 703-305-3230	Telephone No. (703) 305-5163

Form PCT/IPEA/402 (July 1998)

PILLSBURY WINTHROP
DOCKETING
RECEIVED
MAY 26 2004
McLEAN, VA

PATENT COOPERATION TREATY

From the INTERNATIONAL BUREAU

PCT

NOTIFICATION CONCERNING SUBMISSION OR TRANSMITTAL OF PRIORITY DOCUMENT

(PCT Administrative Instructions, Section 411)

To:

CAWLEY, Thomas, A., Jr.
Pillsbury Winthrop LLP
P.O. Box 10500
McLean, VA 22102
United States of America

Date of mailing (day/month/year) 03 October 2003 (03.10.03)	
Applicant's or agent's file reference 37003-304483	**IMPORTANT NOTIFICATION**
International application No. PCT/US03/19652	International filing date (day/month/year) 23 June 2003 (23.06.03)
International publication date (day/month/year) Not yet published	Priority date (day/month/year) 21 June 2002 (21.06.02)
Applicant IDEC PHARMACEUTICALS CORPORATION et al	

1. The applicant is hereby notified of the date of receipt (except where the letters "NR" appear in the right-hand column) by the International Bureau of the priority document(s) relating to the earlier application(s) indicated below. Unless otherwise indicated by an asterisk appearing next to a date of receipt, or by the letters "NR", in the right-hand column, the priority document concerned was submitted or transmitted to the International Bureau in compliance with Rule 17.1(a) or (b).

2. This updates and replaces any previously issued notification concerning submission or transmittal of priority documents.

3. An **asterisk(*)** appearing next to a date of receipt, in the right-hand column, denotes a priority document submitted or transmitted to the International Bureau but not in compliance with Rule 17.1(a) or (b). In such a case, **the attention of the applicant is directed** to Rule 17.1(c) which provides that no designated Office may disregard the priority claim concerned before giving the applicant an opportunity, upon entry into the national phase, to furnish the priority document within a time limit which is reasonable under the circumstances.

4. The **letters "NR"** appearing in the right-hand column denote a priority document which was not received by the International Bureau or which the applicant did not request the receiving Office to prepare and transmit to the International Bureau, as provided by Rule 17.1(a) or (b), respectively. In such a case, **the attention of the applicant is directed** to Rule 17.1(c) which provides that no designated Office may disregard the priority claim concerned before giving the applicant an opportunity, upon entry into the national phase, to furnish the priority document within a time limit which is reasonable under the circumstances.

Priority date	Priority application No.	Country or regional Office or PCT receiving Office	Date of receipt of priority document
21 June 2002 (21.06.02)	60/390,191	US	30 Sept 2003 (30.09.03)

The International Bureau of WIPO
34, chemin des Colombettes
1211 Geneva 20, Switzerland

Facsimile No. (41-22) 338.70.10

Authorized officer

Farid ABBOU

Telephone No. (41-22) 338 8169

PATENT COOPERATION TREATY

From the INTERNATIONAL BUREAU

PCT

INFORMATION CONCERNING ELECTED OFFICES NOTIFIED OF THEIR ELECTION

(PCT Rule 61.3)

To:

CAWLEY, Thomas, A., Jr.
Pillsbury Winthrop LLP
P.O. Box 10500
McLean, VA 22102
United States of America

Date of mailing (day/month/year) 07 July 2004 (07.07.2004)	
Applicant's or agent's file reference 37003-304483	**IMPORTANT INFORMATION**

International application No.	**International filing date** (day/month/year)	**Priority date** (day/month/year)
PCT/US2003/019652	23 June 2003 (23.06.2003)	21 June 2002 (21.06.2002)

Applicant
IDEC PHARMACEUTICALS CORPORATION et al

1. The applicant is hereby informed that the International Bureau has, according to Article 31(7), notified each of the following Offices of its election:

   EP :AT,BE,BG,CH,CY,CZ,DE,DK,EE,ES,FI,FR,GB,GR,HU,IE,IT,LU,MC,NL,PT,RO,SE,
   SI,SK,TR
   National :BG,CA,CN,DE,IL,JP,KP,KR,MN,NO,PL,RO,RU,SK,US

2. The following Offices have waived the requirement for the notification of their election; the notification will be sent to them by the International Bureau only upon their request:

   AP :GH,GM,KE,LS,MW,MZ,SD,SL,SZ,TZ,UG,ZM,ZW
   EA :AM,AZ,BY,KG,KZ,MD,RU,TJ,TM
   OA :BF,BJ,CF,CG,CI,CM,GA,GN,GQ,GW,ML,MR,NE,SN,TD,TG
   National :AE,AG,AL,AM,AT,AU,AZ,BA,BB,BR,BY,BZ,CH,CO,CR,CU,CZ,DK,DM,DZ,EC,
   EE,ES,FI,GB,GD,GE,GH,GM,HR,HU,ID,IN,IS,KE,KG,KZ,LC,LK,LR,LS,LT,LU,LV,MA,
   MD,MG,MK,MW,MX,MZ,NI,NZ,OM,PG,PH,PT,SC,SD,SE,SG,SL,TJ,TM,TN,TR,TT,TZ,UA,
   UG,UZ,VC,VN,YU,ZA,ZM,ZW

3. The applicant is reminded that he must enter the "national phase" **before the expiration of 30 months from the priority date** before each of the Offices listed above. This must be done by paying the national fee(s) and furnishing , if prescribed, a translation of the international application (Article 39(1)(a)), as well as, where applicable, by furnishing a translation of any annexes of the international preliminary examination report (Article 36(3)(b) and Rule 74.1).

   Some offices have fixed time limits expiring later than the above-mentioned time limit. For detailed information about the applicable time limits and the acts to be performed upon entry into the national phase before a particular Office, see Volume II of the PCT Applicant's Guide.

   The entry into the European regional phase is postponed **until 31 months from the priority date** for all States designated for the purposes of obtaining a European patent.

RECEIVED
PILLSBURY WINTHROP LLP/VA

JUL 21 2004

CL 037003 MT# 304483
ATTY(S)
DUE: N/A
DKT BY (1) mdt

The International Bureau of WIPO **34, chemin des Colombettes** **1211 Geneva 20, Switzerland**	Authorized officer: Emmanuel BERROD (Fax 338 7010)
Facsimile No. (41-22) 338.70.10	Telephone No. (41-22) 338 8389